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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/768,167	02/02/2004	John Brassil	040219.04	6029

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EXAMINER	
SAUCIER, SANDRA E	
ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/768,167	BRASSIL ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 18-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 18-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/16/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16, 18-26 are pending and are considered on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The CITATION of some of the references on PTO 1449 submitted 5/9/08 is incomplete. 37 CFR 1.98(b) requires that each reference be completely identified. See MPEP 707.05(e) III for examples for complete citation of parts of books.

Each publication must be identified by publisher, author(if any), title, relevant pages of the publication, and date and place of publication.

The date of publication supplied must include at least the month and year of publication, except that the year of publication (without the month) will be accepted if the applicant points out in the information disclosure statement that the year of publication is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the particular month of publication is not in issue.

Applicant alleges that applicants do not have to supply a complete citation for each submitted reference. However, the MPEP is clear that in order for a reference to be considered, it must be COMPLETELY identified. The MPEP gives examples of what is considered to be a complete identification, especially with regard to the citation of books and electronic media. The applicant argues that the examples of what is considered to be a complete identification does not apply to the applicant since the examples are given MPEP 707.05(e) II. However, what is considered to be a complete citation for the examiner is reasonably expected to be a complete citation of a piece of art whether listed by the applicant or by the examiner.

The applicant has presented a staggering number of references to be considered, but does not, in return, fulfill the applicant's burden of complete identification of each reference submitted.

The French documents, 1, 2 still lack an explanation of relevance. The search report is merely a citation of the document, it does not give an English abstract or a statement of relevance by the individual designated in § 1.56(c) most knowledgeable about the content. The search report merely gives the citation of the foreign patent without a statement of relevance.

Citation 3 lacks the journal name in which the proceedings were published. The reference of citation 6 is still illegible. Citation 12 and 18 lack inclusive page numbers. Citation 12 also lacks a journal name. Citation 17 appears to be a book, but lacks the name of the book. Citation 18 lacks an author and page numbers. Citation 22 lacks the name of the book or journal.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing elements will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a

nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16, 18-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-47 of copending Application No. 11/802064. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping and coextensive in scope.

Claims 1-16, 18-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 11/802059. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping and coextensive in scope.

These are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

INDEFINITE

Claims 8, 13-15, 18-22, 24, 26 remain/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13-15 recite that "the sensed characteristics relate to ...". It cannot be determined what degree of relationship is required because all characteristics of the organ may be said to be related to one another as the

organ is an isolated, discrete functioning unit and is being maintained in a metabolically active state. There is no nexus between the "sensed" characteristic and the relationship to the parameter of organ viability.

Sensing as recited in claim 8 and 18, 24, 26 may be done by a human in a non-empirical manner. Thus, the claims appear to be open to a visual monitoring or a more or less vague perception or impression of the operator which may be interpreted as "sensing". Thus, it is uncertain what the metes and bounds of the claimed method are and if they are fully supported over their entire scope by the disclosure of the specification.

Claims 19-22 depend ultimately on claim 1. Claim 1 requires that the organ is not suitable for transplantation. However, the dependent claims state that the organ was preserved in condition for transplantation, or is suitable for transplantation. Thus these claims do not further limit the independent claim.

Response to Arguments

Applicants argue that all is explained in the specification and that one of skill in the art would know everything, but without explaining the metes and bounds of the terms which can have different plain meanings. Thus, the arguments are unpersuasive of error in the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 18-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification states on page 30 that pH, pO2, pCO2, LDH, T/GST, Tprotein, lactate, glucose and ionized calcium levels may be measured along with vascular resistance which are direct measurements of pressure and flow. Base excess is also mentioned, but it is not clear how this differs from pH, especially since no units of measurement are given in the specification. Organ viability index is mentioned in the specification, but how to compute it is not disclosed. In figure 31, temperature, pressure and flow sensors are mentioned. While temperature, pressure, flow and pH sensors are known and have been incorporated into perfusion devices in the past, there is no description of sensors which monitor LDH, T/GST, Tprotein (whatever these abbreviations stand for), lactate, glucose and calcium ion (not total electrolyte concentration) and how to physically incorporate them into the instant perfusion drug test method.

For example, no disclosure of the construction of these sensors or where they are purchased is included in the specification. There are no exemplifications of the claimed method in the specification. The "exemplification" is merely prophetic and is parsed in permissible language, “may be”.

There is no description of what constitutes suitability or non-suitability for transplantation based on the data gathered, i.e. what type of data, how is the determination as to suitability or non-suitability made, what is indicative of organ viability.

It is deemed that the prophetic disclosure does not constitute a proper written description because of the lack of a working example and sufficient detail to reasonably convey that the inventors were in possession of the broadly claimed invention.

ENABLEMENT

Claims 1-16, 18-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while perhaps being enabling for monitoring pH, flow rate, pCO_2, pO_2, pressure of the perfusion liquid and temperature of the

perfusion liquid by sensing, i.e. with sensors, does not reasonably provide enablement for sensing glucose (concentration?), lactate (concentration?), Tprotein (concentration?), T/GST (? concentration?), base excess, etc. in a method of testing a compound while perfusing an organ. No explanation of the nexus between the analyses of a parameter and the determination of the suitability for transplantation has been given. No nexus between the type of data gathered and the relationship to absorption, distribution, metabolism, excretion, pharmacokinetics, pharmacodynamics, toxicity, etc. is taught.

The claims are broadly directed to determining the effects of a test substance on an organ in a perfusion method by "gathering data regarding the organ and the test substance and interaction between the organ and the test substance".

There is no actual working example, only prophetic statements are made.

The perfusion of an organ requires a mechanical device of some sort which must be compatible with the "sensors" which sense the change in concentration of the individual compounds which are interacting with the organ and/or which the organ is releasing in response to the test compound, which are in the thousands if not millions and which could be in a perfusion liquid being perfused through an organ and which sensors can relay this information in a recognizable manner to an operator.

However, the specification lacks the description of such sensors which can sense T/GST protein, for example, or C-reactive protein or endothelial cells (damage to the endothelial lining @ pages 6 and 7) and which can be incorporated into a mechanical device, which is inherently required by the use of the term, perfusing.

Also, there is no disclosure of what the "sensed characteristics" relate to. Use of the words, absorption, distribution, metabolism, excretion and pharmacodynamics etc. do not explain the relationship between the drug to be

tested and the results to be sensed by a sensor as a result of the drugs effect on the organ. Thus, there is no nexus between the test substances effects and the data to be recorded by a sensor, which is both not stipulated and not described.

Furthermore, there is no description and no nexus between the data collected and the term, “organ viability” or between "analyzing the organ" and the determination of suitability for transplantation. No information is given in the specification that directly relates organ viability and an type of sensor, for example does the pO_2 increase or decrease with an increase or decrease in organ viability. No information is given with regard to the specifics of the nexus between analyzing an organ and its suitability for transplantation.

The application does little more than outline goals applicants hope the recited invention achieves.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim Rejections - 35 USC § 103

Claims 1-16, 18-26 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 94/06292 [IDS] in combination with WO 94/06292 [N], WO 96/298865 [IDS] and Wiley *et al.* [U] or Nakahara *et al.* [V] and The Handbook of Human Tissue Sources [U1] in light of the statement of the National Center of Research Resources [V1].

The claims are directed to a method of testing substances on an organ comprising: analyzing whether the organ is suitable for transplantation and if not suitable, perfusing the organ with a first medical fluid, “exposing” the organ to a test substance, gathering data. Dependent claims require the use of two medical fluids and the testing of an immunotoxin.

The primary reference lacks the analysis of the organ to determine if it is suitable for transplantation and the use of organs that are specifically not suitable for transplantation in the disclosed test method.

WO 94/06292 discloses a method of organ perfusion where physiological or pharmacological research, i.e. effects of compounds, may be performed on an organ. Upstream sensors and downstream sensors monitor the perfusate for characteristics of pH, electrolytes and other characteristics. The sensors generate signals and are transmitted in real time, stored for future analysis or both (page 12). Duplicate organs may be perfused with perfusate that differs in only one component (pages 15 and 17). The effect of the component may be measured by the characteristics of the perfusate or other means. There is no limitation on the condition of the organ with respect to suitability for transplantation.

WO 98/09166 discloses a method for perfusing an organ with a blood substitute, administering test compounds, analyzing the perfusate for the concentration of the test compounds, thereby determining the ability of the organ to effect absorption, metabolism and excretion of the drug. There is no limitation on the condition of the organ with respect to suitability for transplantation.

WO 96/298865 teach the use of two perfusates in a method of organ perfusion. The first is a crystalloid solution and the second is a blood based solution (pages 26, 27). Thus, it is known to perfuse an organ with a first fluid to remove residual blood and other fluids and then with a second fluid which is a blood based fluid. Also, pharmaceutical and physiological agents may be perfused (page 6).

Wiley *et al.* teach perfusion of an organ with two immunotoxins in a transplantation model.

Nakahara *et al.* suggest that immunotoxins might be useful for

pretreatment of organ allografts.

The perfusion of an organ with an immunotoxin in the method of WO 94/06292 which teach the testing of compounds in an *ex vivo* organ perfusion method would have been obvious because such immunotoxins may be valuable in organ transplantation methods as described by Wiley *et al.* or Nakahara *et al.* and thus may be tested in the method described in WO 94/06292 which invites the use of test compounds for research.

Further, the method of WO 94/06292 may be modified by the use of two distinct medical fluids as described in WO 96/298865 in the absence of evidence of criticality.

Also, the method of WO 94/06292 may be modified by the use of testing of the perfusate by the methods taught in WO 98/09166 which teach analysis of the test compound in the perfusate by various assay methods, such as HPLC and others.

The Handbook of Human Tissue Sources states that the Human Tissues and Organs for Research unit focuses on the retrieval and distribution of tissue and organs. The website of the Human Tissue and Organ Resource for Research from the National Institutes of Health, states that the unit provides an opportunity for people who wish to become donors, but whose tissues and organs cannot qualify for transplantation and might otherwise be discarded to donate their tissues and organs for research.

Since WO 94/06292 is silent with regard to the suitability or unsuitability for transplantation of the organ to be tested in the described pharmacological method, it can be considered to be open to the use of both these subsets of organs.

The use of an organ which is not suitable for transplantation in a method of research such as the testing compounds in physiological or pharmaceutical

research as taught by WO 94/06292 is well within the purview of one of skill in the art and it is known that banks have been made available to researchers for the express purpose of donating organs unsuitable for transplantation for use in research.

One of skill in the art may use an organ which has been determined to be unsuitable for transplantation in the absence of evidence to the contrary especially because such banks and exchange resources have been instituted for research on such unsuitable organs.

One of ordinary skill in the art would have been motivated at the time of invention to make these substitutions in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Response to Arguments

Applicants argue that the NCRR statement of record is not prior art. This is true. However, the construction of the rejection is "in light of" the statement. Thus, this reference merely more fully explains the National Disease Research Interchange's purpose and function, which Interchange is cited in the Handbook of Human Tissue Sources published in 1999. MPEP states that references cited to show that the characteristics and properties of prior art products were known. In this case, the National Disease Research Interchange's purpose and products are more fully explained than in the 1999 reference which clearly demonstrates that the Interchange existed prior to applicant's filing.

Applicants argue that the references do not teach the steps of analyzing the organ to determine if it is suitable for transplantation, and using the non-suitable organs in the testing procedure. Please note WO 96/29865 teaches that there is a shortage of human donor organs for transplantation (page 1, l. 10). Thus, the use of human organs unsuitable for transplantation for research,

instead of organs suitable for transplantation, especially in view of the established organ/tissue bank of organs unsuitable for transplantation (NDRI), is routine, well known and well within the purview of one of ordinary skill in the art.

Applicants argue that the organs distributed through the HTOR are typically frozen and they are never considered to be suitable for transplantation. First, "typically" is not the same as always. Second, since applicant's argue that frozen organs are never suitable for transplantation, and the organs available from HTOR are typically frozen, this seems to fulfill the "analyzing" step. Third, this argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Counsel's arguments cannot take the place of objective evidence. *In re Schulze*, 145 USPQ 716 (CCPA 1965); *In re Cole*, 140 USPQ 230 (CCPA 1964): and especially *In re Langer*, 183 USPQ 288 (CCPA 1974).

Applicants now argue that there are some claims which use organs which are suitable for transplantation. First, the claims in question are indefinite since the independent claims appear to require the use of organs which are unsuitable for transplantation. Second, since the primary references are silent with regard to whether the organs used in their tests are suitable or unsuitable for transplantation, the references are interpreted to cover both species of organs, i.e. those suitable and those unsuitable for transplantation. In the absence of evidence to the contrary, it is considered that this is within the understanding and abilities of those of skill in the art, see *KSR International Co. v. Teleflex, Inc*. 82 USPQ2d 1385 (2007) at 1396.

Conclusion

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). It is applicants' burden to indicate how amendments are supported by the ORIGINAL disclosure. Please note that a response which does not specifically point out the support for amendments to the claims may be considered nonresponsive, see MPEP 714.02.

Due to the procedure outlined in MPEP 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 USC 102 or 35 USC 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sandra Saucier/
Primary Examiner
Art Unit 1651